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AB An attractive approach to the therapy of solid tumors would be to target cytotoxic agents or coagulants to the vasculature of the tumor rather than to the tumor cells themselves. This strategy has 3 advantages: (a) it should be applicable to many types of solid tumors because all require a blood supply for survival and growth; (b) the target endothelial cells are directly accessible through the blood and are normal cells, making the outgrowth of resistant mutants unlikely; and (c) there is an in-built amplification mechanism because thousands of tumor cells are reliant on each capillary for nutrients and oxygen. Despite its theoretical attractions, the approach of tumor vascular targeting has not been testable because antibodies that recognize tumor vascular endothelial cell antigens with adequate specificity are currently not available. In this study, we developed a model system in which to investigate the antibody-directed targeting of vascular endothelial cells in solid tumors in mice. A neuroblastoma transfected with the mouse interferon-gamma gene, C1300(Mu gamma), was grown in antibiotic-treated BALB/c nude mice. The interferon-gamma secreted by the tumor induces the expression of major histocompatibility complex Class II antigens on the tumor vascular endothelium. Class II antigens are absent from the vasculature of normal tissues, although they are present on B-lymphocytes, cells of monocyte/macrophage lineage, and some epithelial cells. Anti-**Class II antibody administered** i.v. strongly stains the tumor vasculature, whereas an antitumor antibody directed against a major histocompatibility complex Class I antigen of the tumor allograft produces classical perivascular tumor cell staining. This model should enable the theoretical superiority of tumor vascular targeting over conventional tumor cell targeting to be tested.